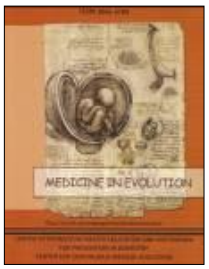
# IMPACT OF COPD ON NUTRITIONAL STATUS

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## ABSTRACT

*A part of patients with chronic obstructive pulmonary disease (COPD) show involuntary weight loss as their disease condition progresses. These patients experience increased of dyspnoea and lower effort capacity than those who do not show weight loss, even when the levels of airflow obstruction are similar.*

*The main loss includes lean body mass (LBM). This may occur even in the presence of the food intake considered to be adequate for the energy expended.*

*A more accurate understanding of the pathophysiology of weight loss and the alterations in the cellular metabolism will help to identify the nutritional approaches.*

***Key words**: COPD, nutritional, lean body mass*

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## INTRODUCTION

Lately, an increased attention has been given to the nutrition aspect in COPD, because weight loss is correlated with increased mortality and a poor prognosis.

Weight reduction associated with COPD has been recognized for a long time by doctors[1] but did not show a particular importance maybe because clinicians have focused on targeted treatment of lung function.

During the last years, COPD is seen as a multi-systemic disease with an important impact on the muscular system, and so, loss of lean body mass (LBM) could be a result of systemic effects of the disease. These effects increase the impact of clinical symptoms: limitation of exercise capacity decreesed quality of life and increased mortality. At least one third of the patients with moderately severe forms of COPD (according to GOLD stages) are malnutrition and the percentage is still growing especially in patients with advanced forms of disease.

Denutrition mechanisms in COPD are multiple: inflammatory status (TNF-α, IL-6), hypoxemia (decreesed protein synthesis, loss of appetite), muscle deconditioning, nutritional education (inadequate diet), depression (loss of appetite), smoking (gastrointestinal disorders)[2], etc.

## THE IMPACT OF THE NUTRITIONAL DEPLETION ON MUSCLE FUNCTION

In few studies, nutritional depletion in relation to respiratory and peripheral skeletal muscle function in outpatients with COPD, investigating body composition using bioimpedance analysis, it had been revealed that nutritional reduction of LBM may also occur in patients with normal weight. These patients underwent physical deconditioning assessed by respiratory muscle strength and exercise capacity[3]. Patients with weight reduction showed lower values for respiratory and peripheral skeletal muscle strength but the difference was more pronounced in peripheral skeletal muscles. Also the transfer factor (DLCo) was significantly lower in the group that showed muscle depletion than in patients with normal weight.

## MALNUTRITION / CACHEXIA

Body weight is divided into two main compartments: fat body weight and lean body mass, the latter containning mainly the skeletal muscle mass. Recent studies suggest that the LBM index brings more complex information than BMI. Loss of skeletal muscle mass is the main cause of weight loss in COPD. Long denutrition is correlated proportional with: reduced muscle mass and strength, prolonged recovery time after exercise and degradation of life quality.

Patients with COPD present a high degree of sedentary (inactivity) life. In COPD, muscle loss occurs in approximately 20-40% of the patients and is an important predictor of increased mortality. Extreme inactivity may enhance the cachectic phenomenon and in this way some studies have found that cachectic COPD patients show a high activity of protein degradation pathways [4,5].

Cachexia in patients with COPD is multi-factorial and is based on poor

nutrition, increased metabolic rate, hypoxemia, inactivity, oxidative stress, systemic inflammatory process and anabolic hormonal insufficiency. In a study that took into account differences in body composition, Schols et al.[6] showed that the survival average was reduced to half in cachectic patients suffering of COPD (from 4 years to about 2 years). There are no currently conclusive studies showing that cachectic phenomenon is reversible.

It is also possible that some of the patients experience an accelerated aging.

Aging is associated with LBW mass loss[7] and it is possible that those subjects with COPD who developed cachexia to also present an accelerated aging with accelerated loss of LBW.

## MARKERS FOR NUTRITIONAL ASSESSING

For monitoring and evaluation of nutritional status we can use anthropometric indices (most used is BMI, skinfold calipers), indices measured using bioimpedance analysis (LBW, FBW, total water), laboratory analysis tests (less used), multidimensional instruments (MNA - 6 screening questions).[8] Prognostic power in the assessment and monitoring of disease increases when these indices are used together in a composite system. For example, BODE composite index (composed of BMI, 6 minutes walking test, $FEV_1$ and dyspnea measured by MRC scale) has a much better prognostic power than other simple indicators. These indicators taken individually present a weaker prognosis for survival than a BODE type composite index.

## THE ROLE OF FOOD AND NUTRITIONAL SUPPLEMENTS

Several studies have attempted to improve muscle function in COPD patients in terminal stage by nutritional addition, but failed to demonstrate a clinically significant effect.

Recent studies in patients with severe COPD show that muscle oxidative metabolism may also be affected independently of muscle mass wasting [9, 10, 11]. Pathophysiology mechanisms which result in weight loss for patients with COPD are not well understood.

Multiple hypotheses include dietary intake, increased consumption with rest energy, diet inducing thermogenesis, tissue hypoxia and medications.

Given this negative association between COPD and weight loss, a number of clinical trials have examined the influence of dietary supplements, alone or in combination with anabolic substances such as steroids or growth hormone (GH) in patients with COPD.

A meta-analysis that included clinical studies regarding nutritional supplementation in patients with COPD identified nine studies in which nutritional supplementation was compared with standardized clinical treatment (according to GOLD). Nutritional supplementation was defined as caloric supplementation for at least 2 weeks. For each of the outcomes studied (anthropometric measurements, lung function, respiratory muscle strength and functional exercise capacity) the effect of nutritional support was homogeneous, reduced[12].

In another meta-analysis were reviewed prospective randomized clinical trials that included studies that address the immediate effects of a meal, the short term addition (two

weeks), supplementation on more than 2 weeks and supplementation by adjuvant treatments such as anabolic steroids and GH. It was noted that immediately after a high in carbohydrates (CHO) meal, increases the production of carbon dioxide (CO2) and respiratory coefficient (RQ = VCO2 / VO2) and decreases the exercise capacity. Increased $CO_2$ production and ventilation requirements were more pronounced after ingestion of a big CHO load compared with a high level of fat. When a high-fat meal was compared with a moderate-fat meal, the first was associated with a measurable delay in gastric emptying [13, 14]. Such a delay could have, by extending the abdominal distension, a negative impact on the position and the mobility of the diaphragm and chest wall.

Absorption and food metabolism lead to an increase in $CO_2$ production. Given the close relationship between $CO_2$ production, ventilation and intake of high CHO food thus increasing ventilatory requirements. In healthy subjects, increased $CO_2$ is easily removed by increasing alveolar ventilation but in COPD patients this kind of increases contribute to increased dyspnea and $PaCO_2$ and decreased exercise tolerance. Studies that have used anabolic steroids and GH (besides a caloric intake corrected) showed a higher increase in LBW compared to those who received only nutritional supplements in which weight gain was predominantly due to an increase in fat mass. Also it has been observed a small increase of PImax.

Ferreira et al.[15] observed that, while administering a synthetic derivative of testosterone for 6 months to a male group of patients with COPD with malnutrition, an improvement of the LBW malnutrition index, thigh and arm muscle circumference growth. However, the exercise capacity was not significantly different compared to that of the control group. Burdet et al.[16] administrated recombinant human GH (rhGH) and observed an increase in LBW but there was no effect on respiratory muscle strength, peripheral muscle power and dyspnea feeling.

## MUSCLE INDICES WITH PREDICTIVE VALUE ON COPD

In clinical practice we try to continue testing various indices to discover a fundamental relationship between muscle function and the monitoring of disease. PImax is one of these indices.

In a study conducted in our clinic we found that respiratory muscles value will decrease depending on the degree of the disease. The disease degree is more advanced as the value of respiratory muscles (both inspiratory and expiratory muscles) is lower.[17] In COPD patients the LBW loss correlates with the decrease in bone density. Another marker that has shown its prognostic value is the value obtained in the walking test (6MWT). It has been observed a strong correlation between the walking test and the degree of COPD.[18]

Lately, it was noticed that the cross area of the medium thigh muscle is a better predictor of mortality than BMI index in COPD patients. Although, body weight is a useful prognostic marker of COPD, it has some limitations in estimating the muscle mass. Body weight is not sensitive to changes in body composition despite the decline in muscle mass.[19] The dissociation between body weight and muscle mass can be found in obese subjects or in patients with water retention (e.g.

cardiac subjects). Under these conditions the loss of muscle mass may also be replaced as weight intake with fat tissue or fluid retention. This is an additional argument for the use of LBW index for an objective assessment.

In a study by Karine Marquis et al.[20] on 142 patients with COPD, it was performed muscle CT through the quadriceps. Patients were monitored for up to six years to study the relationship between muscle mass and other clinical parameters and also calculation of death risk. By multivariate prediction analysis it was found that thigh diameter measured by CT was variable in the strongest inverse relationship with mortality.

$FEV_1$ (in addition to thigh diameter) was another variable with a statistically significant relationship with mortality. A cut-off diameter of CT <70 $cm^2$ was associated with a four times increase higher with mortality rate, independent of any other variables.

## IMPACT OF PULMONARY REHABILITATION ON MUSCLE FUNCTION

Specific training consisting in rehabilitation exercises is recommendded as a therapeutic strategy that could attenuate the loss of muscle mass (in all patients) but also the reactivation and toning of muscle fibers (in patients that do not show muscle loss).

Are not yet available conclusive studies demonstrating that in cachectic patients, pulmonary rehabilitation can improve skeletal muscle loss. Taking into account the pathophysiology issues it has been proposed a hypothesis accordind to which the cachectic patients respond poorly to a pulmonary rehabilitation program in terms of muscle fiber remodeling.

Vogiatzis I et al.[21]concluded that although skeletal muscle training produce a greater peripheral muscle phenotypic adaptation in non-cachectic patients with COPD compared to that of the cachectic pactients. Patients that suffer from cachexia retain peripheral muscle remodeling capacity (as a response to rehabilitation) and are able to increase their effort capacity in the same extent as patients who do not suffer from cachexia do.

In conclusion, by analyzing various studies[17] we can say that, through pulmonary rehabilitation we can:

- obtain an increase in exercise capacity;
- 6 min walking test (6MWD) is improved by 10-25%, which corresponds to an increase of 50-80 m in the walked distance;
- obtain an endurance of minimum 10 min in treadmill walking or at least 5 min at cycle ergometry performed at submaximal effort;
- 30 min endurance / session of the respiratory muscles subjected to an effort of 30-35% of PIma ;
- for the same intensity of the exercise there is a reduction in ventilation, in lactacidemia and an improvement of the oxidative enzyme activity.
- there is a weight gain of more than 2 kg / 8 weeks at underweight patients.
- reduce the sensation of dyspnea during exercise.

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